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Present and future incidence of dengue fever in Ecuador nationwide and coast region scale using species distribution modeling for climate variability's effect

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ABSTRACT

Dengue fever, a vector-borne disease, represents a priority public health problem in Ecuador. Previous studies indicated that the ecology of the transmitter vector (*Aedes aegypti*) is influenced by environmental parameters and human behavior; however, the effects of those variables on mosquito population dynamics depend on local environmental features. In this study, we identified the most important factors influencing the risk of dengue virus infection in Ecuador. The maximum entropy algorithm (MaxEnt) was used to determine the areas with a high probability of the presence of *Aedes aegypti* under current and future (2050) climatic conditions, using the location of reported dengue cases and potential environmental factors. The model performance was quantified based on an accuracy assessment. Additionally, we used meteorological data from the study period in a partial least square regression (PLS-R) to predict the number of total dengue cases (TDC) and then estimated the future number of cases using the equation obtained with the PLS-R. Population density, elevation, and mean temperatures of the warmest and wettest quarters were found to be the most important variables influencing the mosquito's geographical distribution. Maximum temperature and minimum temperature were the climatic factors with the best projecting capacity in predicting the TDC in the Ecuadorian coast region. The results show a greater mosquito presence probability in populated areas, with a considerable expansion of suitable habitat across the central and southern provinces by 2050. The temporal analysis revealed that the regional dengue outbreak season goes from March to June, and the future estimation predicted that the next large outbreak would occur in 2018. These results present a good intel for solutions of reduction of dengue cases in the country. This further will allow the responsible authorities to pinpoint proper vector control measurements by province.

1. Introduction

Dengue fever is one of the most extensively spread vector-borne diseases in Latin America and the Caribbean, where low-income countries are particularly susceptible to its effects due to social, cultural, economic, and environmental factors (Stewart-Ibarra et al., 2013; Heydari et al., 2017). *Aedes aegypti* and *Aedes albopictus* are the primary vectors transmitting the dengue virus in rural and urban areas around the world (Fatima et al., 2016). In Ecuador, dengue fever became evident after the introduction of serotype DEN1 in 1988 and gained strength after the entry of serotype DEN2 in 1990 and DEN4 in 1993 (Real-Cotto et al., 2017). In 2000, the introduction of serotype DEN3 and the Asian genotype of DEN2 was reported. Since then, the number of severe cases has increased, initially in adults and later in children (Alava et al., 2005). The transmission of dengue fever is considered as endemic throughout the year, showing epidemic cycles that usually coincide with the rainy season, when conditions favor accelerated vector reproduction (Ministerio de Salud Pública, 2013; Jácome et al.,

Abbreviations: AUC, area under the curve; MaxEnt, maximum entropy algorithm; PCA, principal component analysis; PLS-R, partial least square regression; ROC, receiver operating characteristic curve; SDMs, species distribution models; TDC, total dengue cases; Tmax, maximum temperature; Tmin, minimum temperature; VIF, variance inflation factor; VIP, variable importance in the projection

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2019).

Studies have demonstrated that mosquito population dynamics are influenced by climate variability (Chowell and Sanchez, 2006; Chowell et al., 2011), which affects larval growth, adult biting rates, gonotrophic development, and the extrinsic incubation period of the virus in the mosquito (Stewart-Ibarra et al., 2013). The geographic distribution and life cycle of the major vector (*Aedes aegypti*) are climate sensitive; mosquito-borne diseases are thus strongly associated with environmental factors (Karim et al., 2012; Fatima et al., 2016). However, issues such as climate change, socioeconomics, settlements, globalization, and viral evolution can also influence the spread of dengue, which can be worsened by inadequate disease surveillance, difficulties in diagnosis, and low levels of reporting (Anne et al., 2013).

Climate can influence the dengue vector in diverse ways. A heavy rainfall can increase the availability of habitat for juvenile mosquitos, but it can also flush away eggs and larvae from containers, whereas drought can influence mosquito abundance through water storage in houses (Stewart-Ibarra et al., 2013; Naish et al., 2014). On the other hand, high temperatures can reduce the viral incubation time and increase mosquito mortality (Naish et al., 2014). In order to analyze those patterns, the spatial and temporal suitability for dengue fever can be mathematically modeled using species distribution models (SDMs) and machine learning techniques, where occurrence records and environmental variables are integrated in the context of transmission modeling to propose future public health interventions and surveillance systems.

Several studies have determined the climatic suitability for mosquitos in tropical and subtropical regions around the world to identify priority areas for vector control actions and surveillance systems (Mweya et al., 2013; Cardoso-Leite et al., 2014; Fischer et al., 2014; Kraemer et al., 2015; Fatima et al., 2016; Koch et al., 2016). In South America, Chowell et al. (2011) analyzed differences in the timing of dengue epidemics between two geographical regions in Peru, and found that they were potentially connected with the timing of the seasonal cycle of mean temperature. Arboleda et al. (2011) compared two models to map the ecological niche and dynamics of breeding sites for *Aedes aegypti* in Bello, Colombia. In Ecuador, Stewart-Ibarra et al. (2014) studied the dengue vector in urban sectors of the Ecuadorian coast to assess the influence of social and climatic factors, especially during outbreaks. However, a national scale study is needed in Ecuador to enable preventive actions in areas with a greater probability of dengue infection.

In this study, we implemented a spatial analysis using the maximum entropy algorithm (MaxEnt) to identify mosquito-suitable habitat (and thereby the areas at risk of infection) using current and future climatic conditions. A comparative evaluation of the model performance was carried out at the national and coast-region levels to select the most accurate model, assess collinearity issues, and determine whether microclimatic variability across the Ecuadorian highlands (Andes Mountains) influences model performance. Complementarily, we applied a partial least square regression (PLS-R) to acquire a temporal analysis and assess the climatic factors that influence dengue cases in the coastal regions of Ecuador, developing an outbreak prediction model for each coastal Ecuadorian province.

2. Material and methods

2.1. Study area and presence records

This study focuses on a national scale as a first analysis, and on the coast region of Ecuador as a second analysis since this is the region with more influential climatic variables affecting the occurrence of dengue cases (Stewart-Ibarra et al., 2013). Ecuador is a country with tropical characteristics based on its latitudinal location (Fig. 1); however, its three clearly identified regions have climatic and microclimatic variability based on their geographic features (Pourrut, 1983). The coast region, which is the area most affected by dengue disease, has a humid and tropical climate, with a rainy season that extends from January to May and a dry season from June to December. This region registers the circulation of all four serotypes of dengue virus identified in the country and is considered to be the most affected since dengue re-emerged in the country in 1988 (Stewart-Ibarra et al., 2013).

Dengue has increased during the past decade, even with ongoing vector control interventions (Stewart-Ibarra and Lowe, 2013). Reports of outbreaks or epidemics are registered in approximately 70% of the country (Real-Cotto et al., 2017); however, the total number of dengue cases can vary in each province (Table 1) due to socioeconomic and population features, along with vector ecology and its relationship with local climate and the El Niño-Southern Oscillation (Stewart-Ibarra and Lowe, 2013). In Ecuador, dengue fever is managed by the Ministry of Health through the National Service for the Control of Vector-Borne Diseases, which develops year-round vector control campaigns that intensify leading up to and during the rainy season (Stewart-Ibarra and Lowe, 2013; Real-Cotto et al., 2017). For this reason, our objective in this research is to identify areas for priority attention and determine the climatic factors that influence the spatial and temporal trends of dengue fever in Ecuador.

For this study, the Ministry of Health of Ecuador, which operates a disease surveillance system that collects information about all clinically suspected cases of dengue fever, provided the number of dengue cases without warning signs reported by week in health centers and hospitals in urban and rural areas during 2013, 2014, and 2015. We considered the sites where dengue was reported as records of the presence of *Aedes aegypti*, with a total of 984 points at the national level. For the sites at which occurrences were not georeferenced and only location names were provided, a standard procedure was used to assign coordinates using the GeoNames website (www.geonames.org). The Moran's I method was applied to the dengue fever data using ArcMap 10.1 to test whether dengue cases were randomly distributed in space (Stewart-Ibarra et al., 2014; Jácome et al., 2019), where −1 shows good negative spatial autocorrelation (dispersed), 0 indicates perfect spatial randomness, and 1 proves positive spatial autocorrelation (clustered) (Tu and Xia, 2008; Jácome et al., 2019).

2.2. Environmental variables

Temperature, precipitation, elevation, and population density were used to determine the distribution of *Aedes aegypti*. The annual, seasonal, and intra-seasonal temperatures and precipitation layers were obtained as bioclimatic variables from the WorldClim website (http://www.worldclim.org) (Hijmans et al., 2005), with 1 km of spatial resolution for current and future conditions (projection for 2050). The A2 emission scenario of the Intergovernmental Panel on Climate Change was used to generate the future projection because it is currently considered to be the most accurate (Nakicenovic and Sward, 2000; Cardoso-Leite et al., 2014). A digital elevation model was downloaded from the Consortium for Spatial Information website with 250 m of spatial resolution (Jarvis et al., 2008). The human population density was obtained using WorldPop products (www.worldpop.org.uk) with a spatial resolution of 100 m. All of these environmental variables were resampled using the resample tool in ArcMap 10.1 to provide a spatial resolution of 100 m to all of them.

2.3. Spatial analysis modeling procedure

Species distribution models (SDMs) are the most important tools that have been used widely to predict the suitable habitat of a particular species using either presence or presence and absence data, along with physical and environmental variables assumed to influence its distribution (Alava et al., 2005; Cardoso-Leite et al., 2014; Kraemer et al., 2015; Varela et al., 2015; Moya et al., 2017). SDMs can be vulnerable to variable selection (Porfirio et al., 2014) when they are performed with a large dataset of correlated variables which can result in

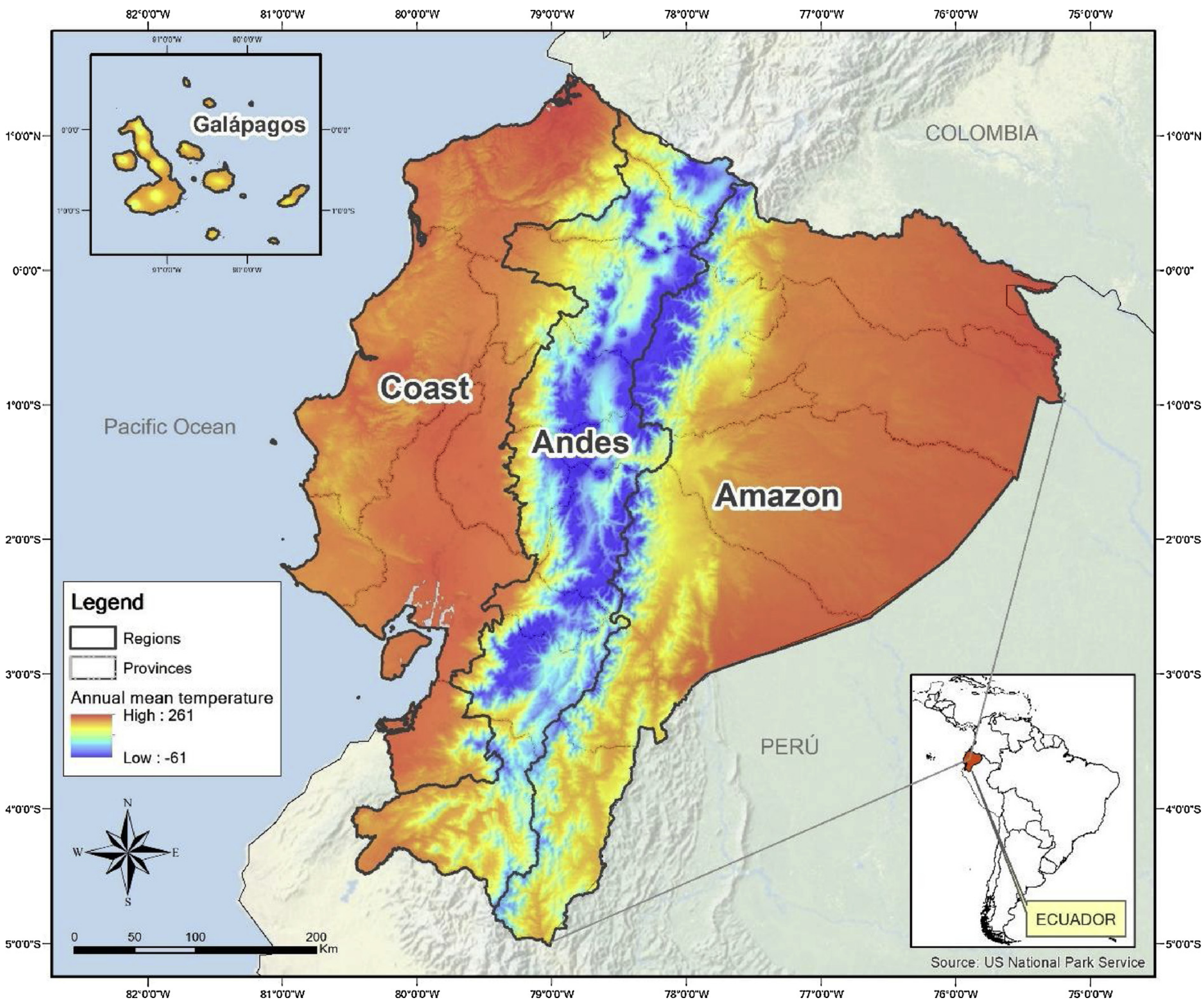

Fig. 1. Regions of Ecuador and their annual mean temperatures with values given in °C*10 (261 = 26.1 °C).

Table 1
Total number of reported dengue cases by province in Ecuador during 2013–2015.

Region	Province	Total number of cases reported			
		2013	2014	2015	Total
Coast	El Oro	1339	2555	5864	9758
Coast	Esmeraldas	510	881	3320	4711
Coast	Guayas	3572	5726	12496	21794
Coast	Los Ríos	1847	1758	2364	5969
Coast	Manabí	2371	2021	12855	17247
Coast	Santa Elena	260	394	700	1354
Andes	Azuay	67	116	107	290
Andes	Bolivar	265	37	29	331
Andes	Cañar	210	125	198	533
Andes	Carchi	4	9	5	18
Andes	Chimborazo	16	37	15	68
Andes	Cotopaxi	28	47	48	123
Andes	Imbabura	35	62	28	125
Andes	Loja	49	28	182	259
Andes	Pichincha	154	167	401	722
Andes	Santo Domingo	213	71	766	1050
Andes	Tungurahua	12	5	7	24
Amazon	Morona Santiago	449	500	16	965
Amazon	Napo	191	107	117	415
Amazon	Orellana	972	191	215	1378
Amazon	Pastaza	17	5	15	37
Amazon	Sucumbíos	1085	186	550	1821
Amazon	Zamora Chinchipe	22	16	51	89
Insular	Galápagos	2	22	184	208

multicollinearity (Moya et al., 2017), a statistical feature that can cause problems in estimating parameters because it expands the variance of regression parameters, possibly generating incorrect identifications in the model (Dormann et al., 2013). In this study, we generated our model at the national level and the coast-region level to observe whether the model performance was influenced by collinearity issues or micro-climatic variability across the Andes Mountains. We constructed a specific model for the coast region because it consistently registers the highest number of dengue cases in Ecuador.

Bioclimatic variables are well known to have a high correlation that can differ spatially (Fatima et al., 2016). Therefore, we used principal component analysis (PCA) to remove multicollinearity, identifying uncorrelated variables through the varimax loading analysis (Dormann et al., 2013; Fatima et al., 2016). The number of principal components (PCs) was selected based on the cumulative variance percentage (Johnson and Wichern, 1992); four PCs showed a variance higher than 85%. We selected the variables with loadings greater than the proportional variance shown by the PCA, 0.473 for the national level and 0.366 for the coast-region level (Table 2), since they represent 10% of variance for the variable being explained by the PC-axes (Dormann et al., 2013). Six variables were selected for the national level, and a set of 13 variables was identified as uncorrelated for the coast-region level. There were developed four models with different specifications. Model 1 used all 19 bioclimatic variables at a national level, model 2 included only the plain non-correlated variables and the physical factors at the national level, model 3 and 4 follow similar procedure for only the coast-region level (Fig. 2). For each model, future suitability was

Table 2
Varimax loading analysis for the first four principal components at the national level and coast-region level.

Abbreviation	National level Description	Coast region level PC1	PC2	PC3	PC4	PC1	PC2	PC3	PC4
Bio01	Annual mean temperature	0.001	0.375	−0.002	0	**0.411**[b]	−0.017	0.044	−0.003
Bio02	Mean diurnal range (Mean of monthly temperature (max – min))	0.065	0.006	**−0.619**[a]	0.029	−0.018	−0.324	**0.439**[b]	0.092
Bio03	Isothermality (BIO2/BIO7) (*100)	−0.15	0.029	**−0.473**[a]	−0.059	0.016	0.024	**0.589**[b]	−0.015
Bio04	Temperature seasonality (Standard deviation *100)	0.17	0.085	0.29	0.076	0.014	−0.168	**−0.519**[b]	0.059
Bio05	Max temperature of warmest month	0.026	0.406	−0.084	0.02	0.334	−0.201	0.013	0.075
Bio06	Min temperature of coldest month	−0.041	0.326	0.109	−0.01	0.344	0.268	−0.112	−0.07
Bio07	Temperature annual range (BIO5-BIO6)	0.185	0.007	**−0.531**[a]	0.078	−0.027	**−0.418**[b]	0.113	0.128
Bio08	Mean temperature of wettest quarter	0.044	0.352	0.037	−0.003	**0.388**[b]	−0.057	−0.165	0.024
Bio09	Mean temperature of driest quarter	−0.047	0.387	−0.028	0	0.352	0.06	0.209	−0.035
Bio10	Mean temperature of warmest quarter	0.019	0.36	0.032	0.005	**0.389**[b]	−0.062	−0.163	0.019
Bio11	Mean temperature of coldest quarter	−0.014	0.382	−0.027	−0.014	0.348	0.065	0.213	−0.016
Bio12	Annual precipitation	−0.272	0.003	−0.014	−0.31	−0.003	0.133	0.013	**0.428**[b]
Bio13	Precipitation of wettest month	0.03	0.01	−0.028	**−0.534**[a]	0.003	−0.008	0.003	**0.497**[b]
Bio14	Precipitation of driest month	−0.472	0.048	−0.007	0.023	−0.002	**0.379**[b]	0.009	0.097
Bio15	Precipitation seasonality (Coefficient of variation)	0.399	0.154	−0.023	−0.038	0.04	**−0.384**[b]	−0.057	0.001
Bio16	Precipitation of wettest quarter	0.014	0.005	−0.014	**−0.530**[a]	0.002	−0.001	−0.001	**0.496**[b]
Bio17	Precipitation of driest quarter	−0.471	0.04	−0.009	0.016	0.002	0.310	0.024	0.089
Bio18	Precipitation of warmest quarter	0.101	−0.011	0.025	**−0.564**[a]	0.017	−0.009	−0.042	**0.513**[b]
Bio19	Precipitation of coldest quarter	−0.462	0.056	−0.039	0.02	−0.057	0.332	0.118	0.047

[a] value greater than 0.473 for the national level, absolute value.
[b] value greater than 0.366 for the coast-region level, absolute value.

obtained using the variables projected for 2050. In this way, we obtained two models, the first one shows dengue fever climatic suitability under current conditions and the second one shows the suitability under future conditions (2050).

Because data showing vector absence are not usually found, we used the MaxEnt software (Phillips et al., 2017) for its capacity to deal with presence-only records (Fatima et al., 2016), which makes it suitable for constructing ecological niche and risk models (Alava et al., 2005; Cardoso-Leite et al., 2014; Moya et al., 2017). MaxEnt is a machine learning technique that shows a probability distribution based on maximizing the entropy subject, with a logistic model output showing the predicted suitability of conditions for the species in each grid cell, ranging from 0 (not suitable) to 1 (suitable) (Fox and Estay, 2016; Koch et al., 2016). To generate the national and coast-region level models, we assigned 75% of the presence records as training data and 25% as test data in the software settings. We used the random seed selection method to ensure that the model used different sets of presence records for training and testing on every replication.

The jackknife test was generated to calculate variable importance, and variable contributions were obtained to identify the single variable most effective in predicting distribution. The model performance was determined using the area under the curve (AUC) of the receiver operating characteristic curve (ROC). This method corresponds to a plot of *sensitivity* versus *1– specificity* and calculates the ability of the MaxEnt model to differentiate between presence and background sites (Phillips and Dudik, 2008; Fox and Estay, 2016; Jácome et al., 2019); where

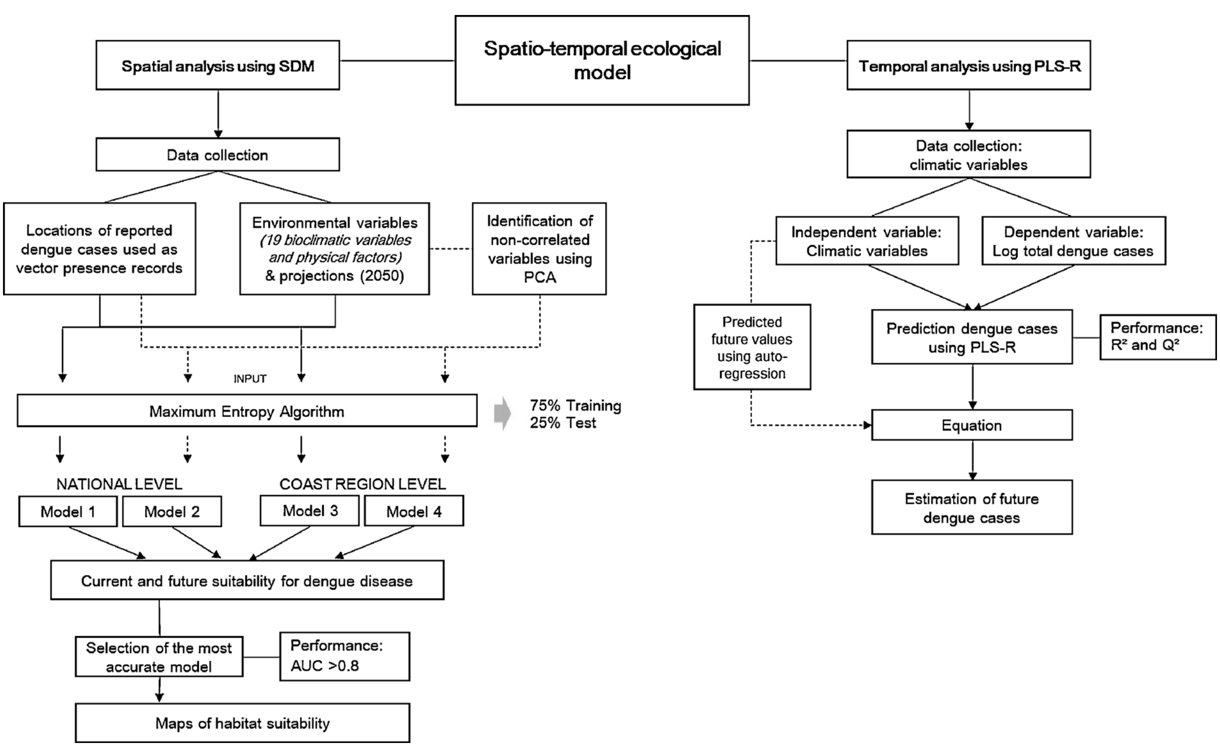

Fig. 2. Generation of the spatio-temporal ecological model.

'*sensitivity*' corresponds to the fraction of observed presences predicted by the model and measures omission errors; and '*specificity*' is the fraction of observed absences predicted as such and measures commission errors (Cardoso-Leite et al., 2014). The AUC value indicates predictive precision using the following categories: excellent (1 – 0.90), good (0.9 – 0.8), acceptable (0.8 – 0.7), bad (0.7 – 0.6), and invalid (0.6 – < 0.5) (Araujo et al., 2005; Jácome et al., 2019). The final maps were generated using ArcMap 10.1.

2.4. Temporal analysis and future estimations

Additional climate data on daily humidity, rainfall, maximum temperature (Tmax), minimum temperature (Tmin), wind speed, sunshine, and cloudiness were provided by the Oceanographic Institute of the Army of Ecuador. The data from four weather stations located across the coastal region are from 2013, 2014, and 2015. Complementary data for the remaining coastal provinces were provided by the National Institute of Meteorology and Hydrology of Ecuador for the same study period. The Galapagos province was excluded from this temporal analysis due to its low rate of dengue cases. Missing weather station data were estimated by interpolation with information from the closest station using the inverse distance weight method in ArcGIS 10.1. This technique gives higher weights to the cells nearest the original values, assuming that objects closer to one another are more comparable than those farther away (Ifaei et al., 2017; Jácome et al., 2018). All data were used in a temporal analysis to identify the climatic factors that influence dengue cases in the coast region of Ecuador, as well as to predict those cases in a PLS-R, which can handle collinearity and is commonly used to analyze a set of dependent variables from a set of independent variables or predictors (Li et al., 2002). The prediction is made by obtaining orthogonal factors (known as latent variables) from the predictors with the most accurate predictive capacity and achieve the least squares regression on those factors rather than on the original data (Helland, 1990; Johnson and Wichern, 1992).

Climatic factors were used as independent variables, and the total number of dengue cases (TDC) was used as the dependent variable in the PLS-R for each province in the coast region. The variables with non-normal distribution were log-transformed to get a better estimate. Because the data showed positive skewness (skewness = 4.44), the dependent variable was also log-transformed for the regression (Karim et al., 2012). The data set was centered and standardized since the variables are not measured on the same units. The accuracy of the model was evaluated using the Q^2 and R^2 of the dependent variable. Values of variable importance in the projection (VIP) were used to identify the factors with the most influence in the models. Those values range in ascending order with values > 1 considered important, and those < 0.5 considered unimportant. Values between 1 and 0.5 inhabit a gray area in which the importance of the variables depends on the size of the data (Eriksson et al., 2001). Model validation was performed with SIMCA software using a permutation validity testing technique. In the training dataset of this method, the independent variables hold intact and the numerical value of dependent variable remains identical but it changes its position randomly. Then another PLS-R is made for the new permutated data where R^2 and Q^2 are calculated using cross-validation with the aim of comparing them with the previous results of model accuracy and examine their significance. The same procedure is run according to the number of permutations that have been selected. (Eriksson et al., 2001; Islam, 2012).

We estimated future dengue cases using the predictive equation generated by the PLS-R. For this, all independent variables were estimated to the year 2020 using an autoregressive model in which a new predictor variable was generated using the original variable lagged by one or more periods based on the quality of the results (significant *p-value* < 0.001) (Faruk and Durdu, 2010; Zarzalejo et al., 2010; Jácome et al., 2019). The auto-regression is expressed by the following equation:

$$y_t = b_0 + \sum_{i=1}^{p} b_i y_{t-i} + e_t$$

where y_t represents the dependent variable values at moment t; $b_i\, y_{t-i}$ are the matrices of coefficients to be calculated and e_t is vector of error terms which are correlated with each other but uncorrelated with their own lags and y_t. The lag length p was set at 12 which correspond to one year of data. (Sadorsky, 2006; Zarzalejo et al., 2010).

3. Results

3.1. Statistical performance of SDMs

The dengue fever presence data were significantly clustered (Moran's I = 0.336; *p-value* < 0.001) with a less than 1% likelihood that this clustered pattern could be the result of chance. Higher concentrations of occurrence and clusters occurred in the coast region than elsewhere. Two models were generated at the national level, model 1 included all 19 bioclimatic variables, and model 2 used the uncorrelated bioclimatic variables identified by PCA and the physical parameters. Two additional models were elaborated using the Ecuadorian coast region as the study area, model 3 used the 19 bioclimatic covariates, and model 4 used the main non-correlated variables; both models 3 and 4 also used elevation and population. The modeling results revealed excellent performance for current conditions and acceptably good performance for the future conditions (2050), according to the AUC evaluation categories (Araujo et al., 2005). However, different results were obtained when the study area was reduced. At the national level, no improvement was observed when collinearity was removed. Model 1 (with all the bioclimatic variables) showed similar spatial predictive capacity (AUC = 0.911) than model 2 (AUC = 0.913), and the two models of future conditions (2050) revealed a better performance for model 1 (AUC = 0.845) than for model 2 (AUC = 0.809). Interestingly, better performance was observed for current and future conditions when the study area covered only the coast region and collinearity was eliminated. This result correspond to model 4 which obtained a training AUC (0.930) higher than model 3 (AUC = 0.923). A similar result was observed in the model of 2050 conditions, model 4 obtained a higher training AUC (0.900) than model 3 (AUC = 0.848). This outcome suggests that MaxEnt tends to perform better in relatively flat areas when collinearity is removed, and that a varied landscape with micro-climatic diversity and steep biogeographic gradients can influence model performance. For this reason and because the coastal region is the most affected by dengue fever, we report only the results obtained with model 4.

3.2. Suitable habitat under current and future climatic conditions

The coast region of Ecuador reported 645 localities affected by dengue fever during 2013–2015, with the provinces of Guayas, Manabí, and El Oro having the greatest number of occurrences. The MaxEnt modeling results revealed a high probability of *Aedes aegypti* distribution across four provinces, Guayas, Los Rios, El Oro, and Manabí (except the north section), under current climatic conditions (Fig. 3a). Esmeraldas and Santa Elena showed a high probability of distribution around areas with high population density. The Galapagos Islands did not show a highly suitable habitat for the mosquito, which matches with its low rate of dengue disease, as shown in Table 1. The mosquito's suitable habitat under the A2 climate change scenario for 2050 reveals an increase in the probability of spatial distribution across the region (Fig. 3b), and the areas currently under a high probability (0.7) of suitability will reach a very high occurrence probability (0.9–1). Thus, the incidence of dengue fever is likely to increase in the peripheral areas around urban centers and in rural areas of Guayas, Los Rios, El Oro, and Manabí.

All variables used to run model 4 were assessed using the jackknife

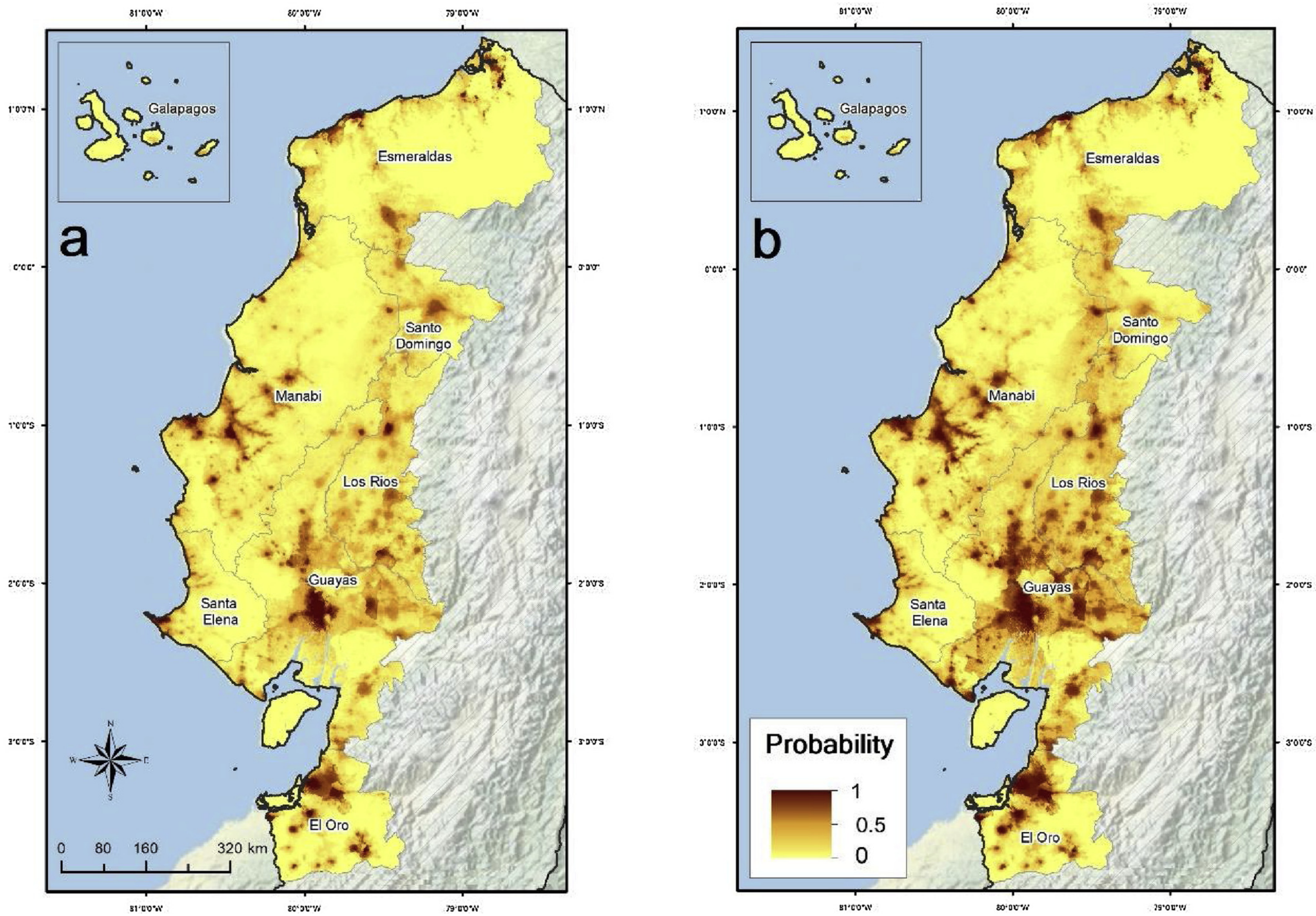

Fig. 3. Maps of potential spatial distribution of dengue fever and suitable habitat for the transmitter vector in the coast region of Ecuador under **(a)** current climatic conditions and **(b)** future climatic conditions (2050).

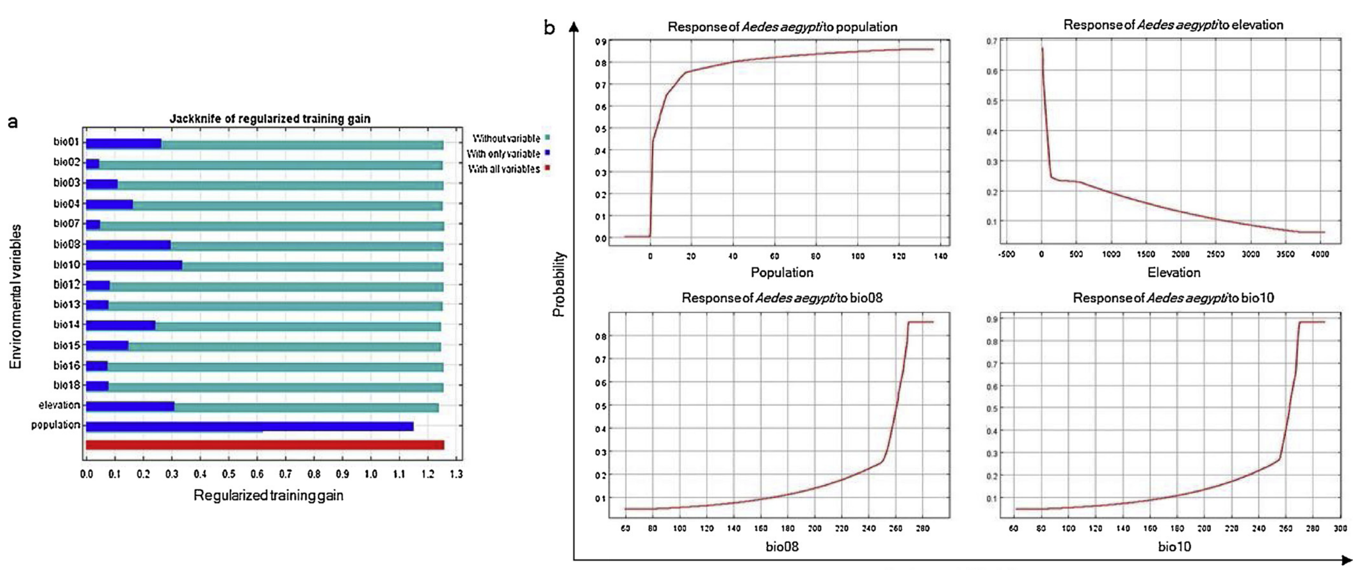

Fig. 4. **(a)** Jackknife test of regularized training gain for *Aedes aegypti* and **(b)** response curves of the one-variable-models for the four most important environmental variables. Values of temperature variables are given in °C*10 (280 = 28.0 °C).

test. Population, elevation, and temperature are the most important variables, as shown by their regularized training gain values (Fig. 4a). Population is the variable that can decrease the gain the most by its omission, reducing it from 1.25 to 0.65. The highest regularized gain among the bioclimatic variables was for the mean temperature of the warmest quarter (bio10), mean temperature of the wettest quarter (bio08), and annual mean temperature (bio01) (Fig. 4a). Thus, temperature plays an important role in mosquito distribution dynamics.

The response curves of one-variable models of the most important environmental variables were additionally identified by the jackknife test. The curves present variations in the probability distribution of *Aedes aegypti* according to each environmental covariate (Fig. 4b). The response curve of mosquito to population probes the increase in mosquito presence as population density increases. Considering elevation, the curve shows that the most suitable habitat in the coast region is in areas with an altitude between 0 and 120 m.a.s.l., with a lower probability of occurrence up to 600 m.a.s.l.; further increases in elevation cause gradual suitability decreases. Populations stabilize in a temperature range of 27 °C – 30 °C for both covariates.

3.3. Climatic factors influencing dengue cases

The TDC reported in the coast region during 2013–2015 varied by year. A similar number was reported for 2013 (n = 10,054) and 2014 (n = 12,321), but many more cases were registered in 2015 (n = 37,239), indicating an outbreak of great magnitude. In each year, dengue cases revealed a specific pattern of occurrence, which is well known to be related to climatic variables. The monthly average of climatic parameters, such as the Tmax, Tmin, humidity, and rainfall, for all the provinces in the coast region are found to influence the dengue outbreaks (Fig. 5). From March, the temperature and number of dengue cases were increased; similarly, while the temperature decreased in the months of June and July, the dengue cases decreased gradually (Fig. 5a). A similar pattern is followed for the parameters of average humidity and rainfall, when these increased about two months before the outbreak periods and finished two months before, the dengue cases began to diminish (Fig. 5b).

The log-transformation of TDC was predicted using PLS-R with monthly climatic data from the study period (2013–2015) for each coastal province. The variance inflation factor (VIF) was applied to assess the multicollinearity of all 7 climatic variables used in the PLS-R for each province. The results present small VIF values, indicating low correlation among variables under ideal conditions (VIF < 10). The standardized residuals of each model ranged between -1.8 and 2.0, suggesting minimal outliers in the dataset. The scatter plots of the standardized residuals versus the standardized predicted values expose a largely symmetrical distribution, suggesting the required constant variance for the models. PLS-R was performed using two latent variables, which accounted for a cumulative variance higher than 90%. The model statistics for predicting Log TDC obtained a Q^2 ranging from 0.411 to 0.558, mean square errors close to zero (indicating a fit appropriate for prediction), and a coefficient of determination R^2 between 0.501 and 0.698 (Table 3). Similar values for R^2 have been obtained in previous research that applied regression methods (Islam, 2012; Karim et al., 2012; Young et al., 2016). The VIP values summarize the importance of the variables in terms of explaining the independent variables and correlating them with the dependent variable (Table 3). The climatic variables obtained different VIP results for each province; however, Tmin and Tmax were important in all of them, which suggests that temperature has an important influence in the mosquito lifecycle in the Ecuadorian coast region. Humidity was important in Guayas, Santa Elena, and Santo Domingo. Rainfall was important in the provinces that reported the highest precipitation during the study period. Interestingly, sunshine was also important in four of the seven coastal provinces.

The regression equation was used to predict TDC, showing that the predicted curve properly follows the intra-seasonal variability of dengue risk in all the provinces, although the model predicted a slightly lower number of dengue cases than was observed during high outbreaks, with the highest at 2015 (Fig. 6). Thus, caution is essential when interpreting results during an outbreak. The observed and predicted TDC for the study period (2013–2015) showed a significant correlation, with Spearman correlation coefficient values > 0.705 and significant p-values ($p <$ 0.05) in all the provinces.

SIMCA software was used to implement a validity testing technique applying 25 permutations for the two latent variables of the seven models. The criteria suggested to check the validity of a model establish that all Q^2 values to the left of the permutations plot must be lower than the original points in the right; or, the regression line of the Q^2-values must intersect the vertical axis at or below zero (Islam, 2012). Considering these criteria, a positive conclusion was made about the validity of the models performed in this study since the plots of each model met the established conditions.

Log TDC was estimated to the year 2020 using an autoregressive model to predict the climatic conditions and putting those predicted conditions into the regression equations previously obtained for each province. The regression plot presented a good model performance (R^2 > 0.89) for all provinces, showing when the outbreaks will occur, rather than just predicting an exact number of future cases (Fig. 7). The most important finding of this approach is that provinces with the highest incidence of dengue fever show the likelihood of a large outbreak during 2018, beginning in March and lasting until August, followed by a regrowth that varies by province. Santa Elena and Santo Domingo, with a low rate of cases, show variability in the estimation, but the highest records occur in months with climatic influences.

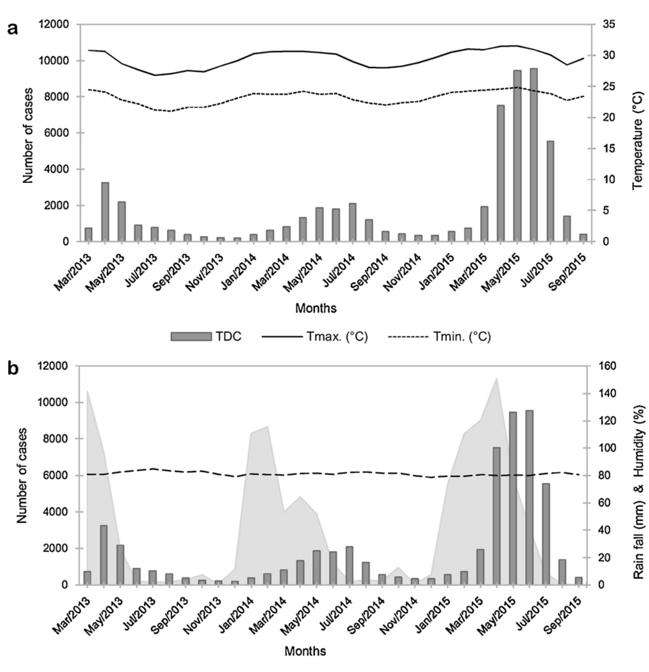

Fig. 5. Monthly average of **(a)** maximum and minimum temperatures, and **(b)** rain fall and humidity in all the coastal provinces compared with the total number of dengue cases reported in the region during 2013–2015.

4. Discussion

Our aim in this study was to investigate the potential spatial distribution of dengue fever and the geographically suitable habitat for *Aedes aegypti* under current and future climatic conditions in Ecuador, as well as to identify the most influential variables over time. Using MaxEnt models, many studies have shown better performance when collinearity is removed (Cruz-Cardenas et al., 2013; Moya et al., 2017; Qin et al., 2017), which we also observed in model 4 for the coast region; however, we did not detect that effect in model 2 at the national level. Our results suggest that removing collinearity is a good option as long as the study area is homogeneous. In addition, data limitations were faced for accomplishing a full spatio-temporal analysis. The temporal dataset of cases of dengue were incomplete in some areas of Ecuador, as the disease was not continuously monitored throughout the

Table 3
Statistics of the prediction of Log TDC during 2013–2015, performed with PLS-R.

	El Oro	Esmeraldas	Guayas	Los Rios	Manabí	Santa Elena	Santo Domingo
R^2	0.698	0.542	0.501	0.609	0.562	0.584	0.513
Q^2	0.558	0.417	0.400	0.544	0.491	0.411	0.438
SD	0.308	0.366	0.349	0.262	0.355	0.437	0.385
MSE	0.086	0.125	0.110	0.064	0.118	0.166	0.133
RMSE	0.292	0.354	0.332	0.254	0.343	0.407	0.364
VIP							
Tmax. (°C)	1.029	1.189	1.438	1.326	1.228	1.083	1.141
Tmin. (°C)	1.246	1.029	1.025	1.320	1.282	1.004	1.556
Humidity (%)	0.138	0.301	1.445	0.837	0.972	1.635	1.931
Rain fall (mm)	0.169	0.485	0.952	1.005	1.136	0.907	0.980
Wind speed (m/s)	1.188	1.576	0.691	0.786	1.030	0.975	0.728
Sunshine (h)	1.123	1.517	0.784	1.116	1.044	0.731	0.771
Cloudiness (octa)	0.532	1.130	0.942	0.984	1.143	0.905	0.814
Coefficients							
Intercept	−10.665	2.388	−13.170	2.291	0.844	−17.111	−14.205
Tmax. (°C)	0.108	0.175	0.115	0.028	0.083	0.038	0.077
Tmin. (°C)	0.189	0.069	0.147	0.032	0.076	0.298	0.186
Humidity (%)	0.006	0.016	0.051	−0.012	−0.013	0.235	0.034
Rain fall (mm)	0.021	0.019	−0.030	0.022	0.051	−0.005	−0.066
Wind speed (m/s)	1.192	−0.194	−0.014	−0.026	−0.048	0.024	0.219
Sunshine (h)	0.165	0.123	0.253	0.032	0.062	0.030	0.142
Cloudiness (octa)	0.053	−0.590	0.014	−0.059	−0.251	−0.640	−0.287

The results represent the statistics for the dependent variable (TDC).
TDC: total dengue cases, SD: standard deviation, MSE: mean square error, RMSE: root mean square error, VIP: variable importance in the projection.

years in the country. Similarly, the spatial dataset of presence of the mosquito species showed missing data at some locations of the country.

However, the spatial analysis showed that the physical factors used in this research are very important to the success of this species in the Ecuadorian coast region. This mosquito is well-known for its close association with human settlements due to the human-blood feeding behavior (Fatima et al., 2016) of its adult females and its preference for tropical climates and low altitudes (Chowell et al., 2011). Elevation, the second most important variable influencing the spatial distribution, is a factor connected with the climatic variables that determine the mosquito's ideal habitat and regulate its physiological behavior. Increasing elevations correlate with a progressive decrease in temperature and variation in rainfall (Fatima et al., 2016), which means that high elevations can act as biogeographic barriers. However, a study conducted in Colombia, an Andean country with geographic features similar to those in Ecuador, reported finding the mosquito at 2,302 m.a.s.l. and infection with dengue virus at 1,984 m.a.s.l. (Ruiz-López et al., 2016), which suggests changes in the distribution patterns of this vector. In the Andean region of Ecuador, the maximum elevation at which the mosquito could be present is 1500 m.a.s.l. (Suarez and Nelson, 1981). Our results also show that *Aedes aegypti* can find ideal conditions up to a mean temperature in the wettest quarter and warmest quarter of 25 °C and 25.8 °C, respectively.

Further research should update and strengthen current and future vector surveillance and control. According to the literature, optimal mosquito development, including breeding sites for egg deposition, occurs in locations with at least 500 mm of annual rainfall and a summer temperature between 25 °C and 30 °C (Medlock et al., 2015), which is consistent with the results of our one-variable response curves, which identified similar ranges for rainfall and temperature during the warmest quarter. Thus, the climatic influence is evident with a 1-2-month lag because mosquitos take 7–45 days to mature from an egg to an adult (Karim et al., 2012). The model for the future panorama in the Ecuadorian coast region contributes to the assumption that dengue vectors will extend their suitable habitat as the climate changes, as has been reported by several researchers (Benedict et al., 2007; Anne et al., 2013; Fischer et al., 2014; Koch et al., 2016). The World Health Organization (WHO) has stated that the endemicity of vector-borne diseases will change, and epidemics could take place in areas where they are presently unusual as a consequence of climate change (WHO, 2012). The most affected areas will be those hitherto unprepared to respond robustly to such events. However, the precision and predictive capacity of models seeking to determine future epidemiological scenarios influenced by climate change remain a source of considerable debate and investigation (WHO, 2012).

Temperature, the most important climatic variable identified by the spatial and temporal analysis, is an essential factor for the mosquito lifecycle that, jointly with humidity, affects both eggs and adults (Gu et al., 2016). The models developed with two components could explain between 50.1% and 69.8% of the variability in the response variables for dengue cases. The results show that the mean temperatures of the wettest and warmest quarters (from the wet and dry seasons, respectively) influence mosquito geographic distribution, and that Tmax and Tmin influence its temporal patterns; Tmin showed a slightly higher importance than Tmax in the VIP values. To date, there is a lack of studies about the ecological modeling of the dengue vector at the national or regional scale in Ecuador; however, a research carried out in the southern coastal city of Machala in El Oro province corroborates our results. The study found that minimum air temperature is a significant regulating climate factor for dengue fever (Stewart-Ibarra et al., 2013; Stewart-Ibarra and Lowe, 2013). They concluded that a gradual increase in minimum temperature caused by global warming could increase the number of optimal transmission days per year (Stewart-Ibarra et al., 2013). In general, an increase in atmospheric temperature would decrease the incubation period, reduce the gonotrophic cycle, and decrease the development rates of immature mosquitoes (Pant and Yasuno, 1973; Stewart-Ibarra et al., 2013; Naish et al., 2014). It would also affect mating behaviors and cause more rapid viral replication and longer mosquito survival (Gu et al., 2016).

Humidity, sunshine, wind speed, cloudiness, and rainfall, in that order, showed lower importance scores in the temporal analysis. Their influence on dengue fever is complex, but they are nonetheless essential in the management of the disease. The high humidity of the rainy season can promote mosquito growth and survival, which could increase the successful propagation of the virus (Wu et al., 2007; Karim et al., 2012). Barbazan et al. (2010) reported that an intensification of mosquito longevity can disproportionately augment the number of potential transmissions by as much as five times when the survival rate rises from 0.80 to 0.95. Relative humidity can also affect mating, oviposition (Wu et al., 2007), and newly-laid eggs, which are vulnerable to

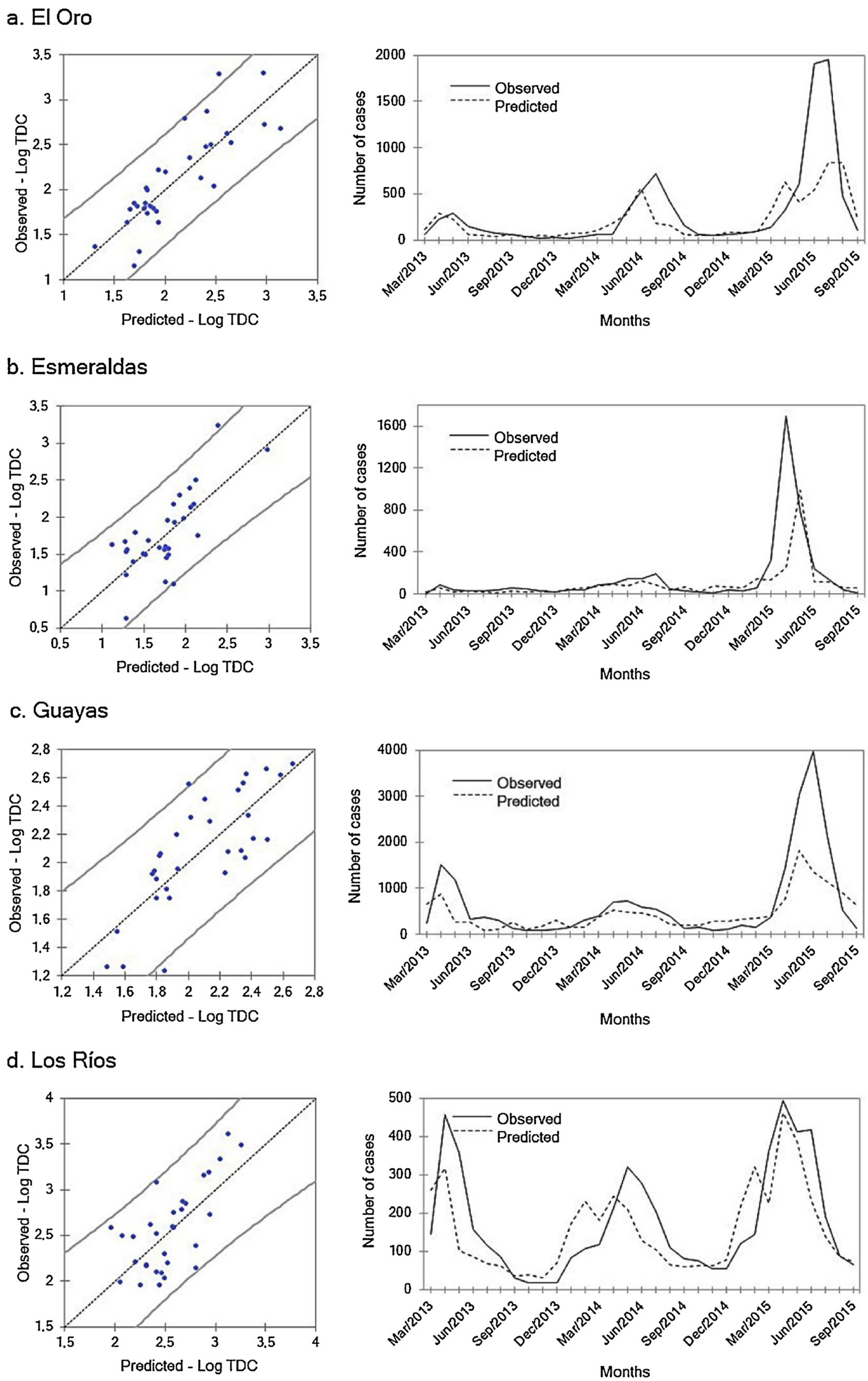

Fig. 6. Prediction of total dengue cases (TDC) during 2013–2015 using monthly climatic data. The graphs on the left side correspond to the regression plot of the predicted log TDC versus the observed log TDC, and the graphs on right side compare the observed and predicted TDCs. The graphs were elaborated for each coastal province: (a) El Oro, (b) Esmeraldas, (c) Guayas, (d) Los Ríos, (e) Manabí, (f) Santa Elena, and (g) Santo Domingo.

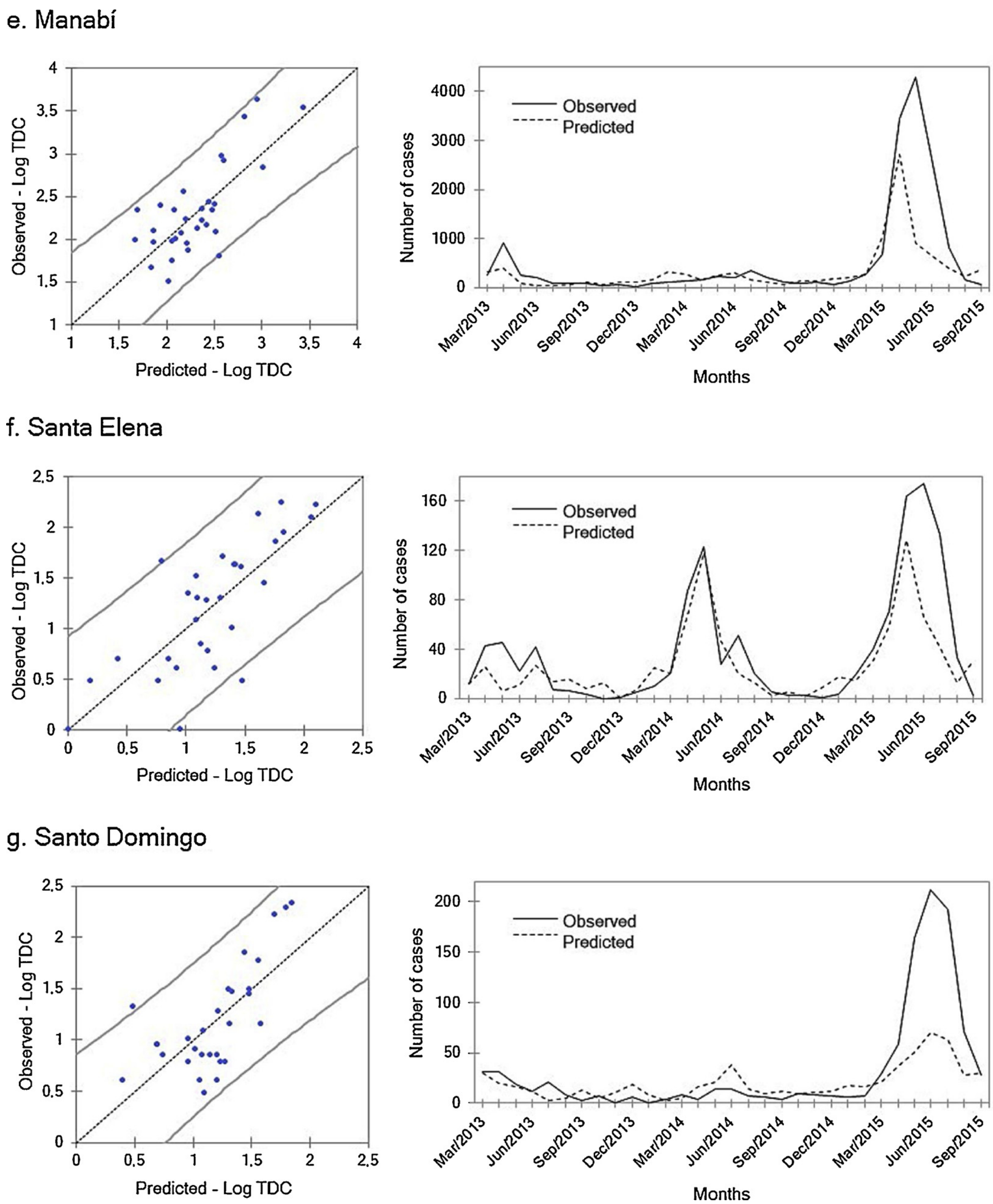

Fig. 6. (*continued*)

desiccation (Gu et al., 2016). The coastal region of Ecuador experiences an increase in sunshine duration from January to June, which matches the increase in TDC. Sunshine can affect the behavior of the vector directly, specifically with regard to its blood feeding during sunrise and sunset (Gu et al., 2016). The wind speed parameter can be associated with rainfall because stormy days usually bring rain and wind together. It’s well known that precipitation and its interaction with human behavior can increase larval habitat through water stagnation, which leads to a proliferation of vector populations (Stewart-Ibarra et al., 2013; Naish et al., 2014).

On the other hand, excessive rain can eliminate habitats through flooding (Wu et al., 2007). However, a study showed that vector population densities were less susceptible to seasonal fluctuations in rainfall in localities where year-round water storage containers are the main mosquito breeding sites (Barrera et al., 2011). Therefore, household water storage is an important contributor to the rise of dengue risk (Stewart-Ibarra and Lowe, 2013). For this reason, a more specific modeling approach is needed to include the specific social and ecological elements that influence *Aedes aegypti* habitat in Ecuador. The climatic variables used in the temporal analysis should remain in the new model using historical and updated data to assess the strength of their associations. We also suggest extending time-series models and include geographical variation and thereby obtain more accurate surveillance information for the coast region. Predictions from such a model could provide an increased lead-time for vector control interventions and develop early warning systems for efficient prevention of dengue fever outbreaks.

5. Conclusion

The areas at risk for dengue virus infection are well established in and around populated areas of the coast region of Ecuador, with a high emphasis in the central and south region. The MaxEnt model projection for 2050 shows an increase in mosquito suitable habitat that would cause a large rise in dengue fever incidence, especially around urban centers and in the rural areas of Guayas, Los Rios, El Oro, and Manabí

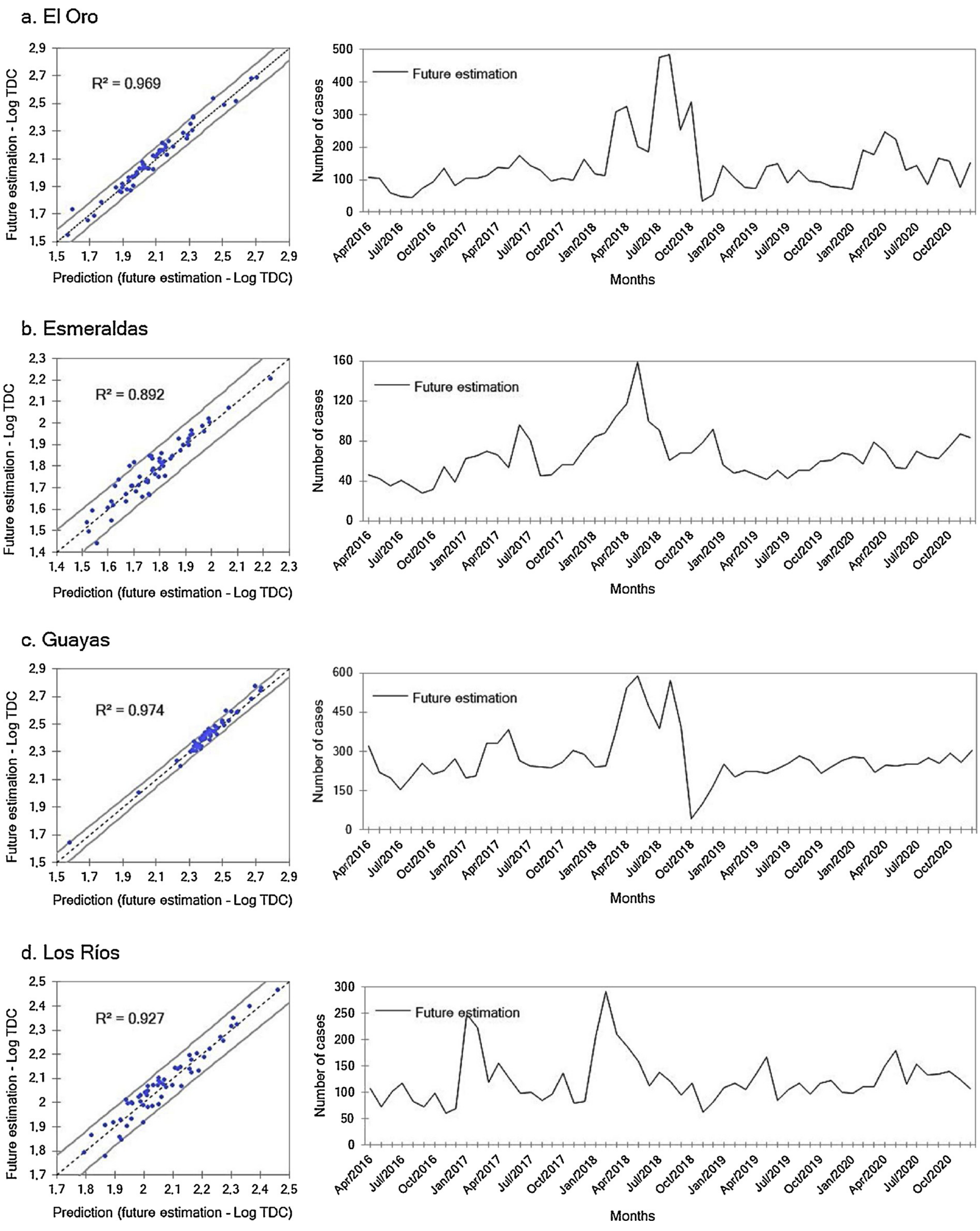

Fig. 7. Future estimation of dengue cases for the year 2020. The graphs on the left side correspond to the regression plot of the future estimation, and the graphs on right side show the outbreaks predicted for the year 2020. The graphs were elaborated for each province in the coast region: (a) El Oro, (b) Esmeraldas, (c) Guayas, (d) Los Ríos, (e) Manabí, (f) Santa Elena, and (g) Santo Domingo.

provinces. Factors such as population, elevation, and mean temperatures of the warmest and wettest quarters were identified as main contributors to the mosquito spatial pattern distribution. A temporal analysis showed Tmin and Tmax to be the most important climatic variables in the prediction of dengue cases. Determining which factors influence the risk of dengue infection is important in controlling the spread of this disease and is essential in the development of predictive models for use as decision support tools and early warning systems. Therefore, Ecuadorian government institutions need to organize and facilitate access to climate, vector, and dengue virus information as a geospatial database to integrate the socioenvironmental factors that influence mosquito habitat and to generate appropriate intervention strategies. The results from SDMs with MaxEnt showed better performance when collinearity was removed and the study area was relatively

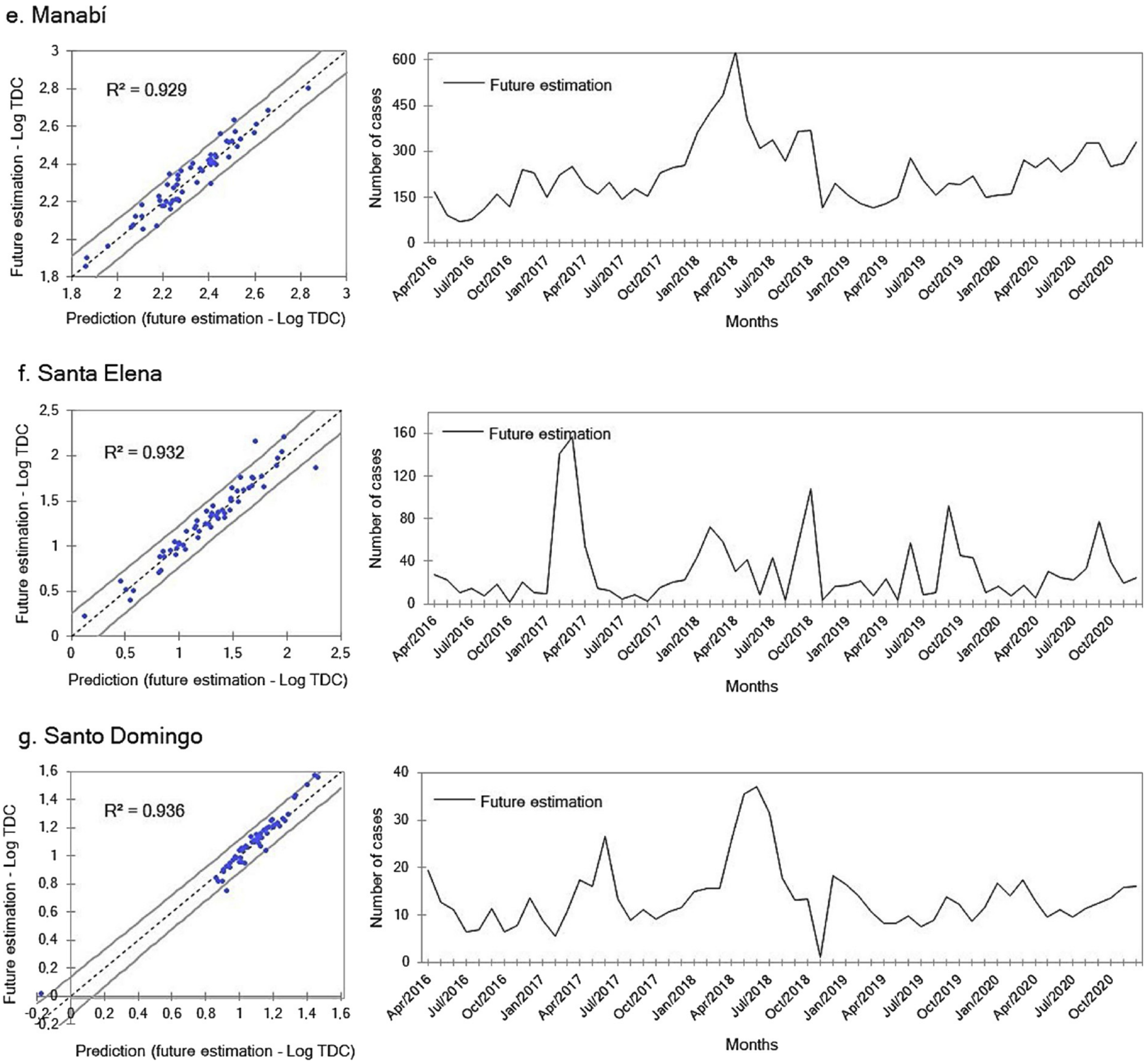

Fig. 7. (*continued*)

flat, which indicates that a large, steep geography with micro-climatic variety can influence model performance when it is part of a wide section of the study area.

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